Hemolytic Uremic Syndrome

Report Immediately

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Hemolytic uremic syndrome (HUS) is a syndrome of anemia, renal injury and low platelet count, for which there are several causes. Among children, the most common cause of HUS is infection with a Shiga toxin-producing organism, most commonly *Escherichia coli* O157:H7 or some other strain of enterohemorrhagic *E. coli* (EHEC). *Shigella dysenteriae* also produces Shiga toxin and infection with this organism can also be accompanied by HUS.

B. Clinical Description

HUS is an acute illness involving the renal system and blood clotting mechanisms. For HUS caused by infection with a Shiga toxin-producing organism, the syndrome will usually manifest itself 3 to 10 days after the onset of a diarrheal illness, often including bloody diarrhea. Approximately 2–7% of cases of enterohemorrhagic *E. coli* (EHEC), such as *E. coli* O157:H7, develop HUS. HUS is a combination of microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure. Thrombotic thrombocytopenic purpura (TTP) is another potential consequence of infection with a Shiga toxin-producing organism. TTP is similar to HUS with more prominent neurologic signs. HUS is most commonly seen in children, whereas TTP is more commonly seen in adults. HUS in children can be fatal. Most cases of HUS, but few cases of TTP, follow an acute gastrointestinal illness (usually diarrhea). **Only HUS or TTP that follows an acute diarrheal illness should be reported.**

C. Reservoirs

While cattle appear to be the most significant reservoir for *E. coli* O157:H7 and other EHEC strains, other animals, such as deer, are also known to carry these bacteria. In contrast, humans are the only known reservoir for *Shigella dysenteriae* type 1.

D. Modes of Transmission

See the chapters on *E. coli* O157:H7 and *Shigella* for modes of transmission for each organism.

E. Incubation Period

Onset of HUS usually occurs 3 to 10 days after the onset of diarrhea. Diarrhea may have resolved and the case may appear to be improving when the onset of HUS occurs. (For the incubation periods of the specific bacteria, refer to the chapters on *E. coli* O157:H7 and *Shigella.*)

F. Period of Communicability or Infectious Period

People with HUS may be infectious if still shedding *E. coli* O157:H7 or *Shigella* in their stool. (Refer to the chapters on each of these organisms for information on their infectious periods.)

G. Epidemiology

HUS is seen worldwide and may occur in 5 to 10% of *E. coli* O157:H7 infections of children under 10 years of age. A bacterial pathogen is often not laboratory confirmed in cases of HUS, and therefore, the proportion of cases of HUS due to specific bacterial infections is difficult to ascertain. Cases of HUS have been attributed to

non-O157:H7 *E. coli* serotypes (*i.e.*, other EHEC strains), but the importance of these other serotypes in the occurrence of HUS is not known at this time.

2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. What to Report to the Massachusetts Department of Public Health

- The onset of acute renal disease within 3 weeks of acute bloody or non-bloody diarrhea.

Note: See Section 3) C below for information on how to report a case.

B. Laboratory Testing Services Available

The Massachusetts State Laboratory Institute (SLI) does not provide laboratory services for diagnosing acute renal disease. However, the SLI, Enteric Laboratory will test stool samples for the presence of *Shigella, E. coli* O157:H7 or Shiga toxins. For more information contact the Enteric Laboratory at (617) 983-6609.

The SLI, Food Microbiology Laboratory (617- 983-6616) will test implicated food items for *Shigella* and *E. coli* O157:H7 from a cluster or outbreak. See Section 4) D, Environmental Measures for more information.

3) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- HUS has been clearly demonstrated to be an important sequelae of infection with *E. coli* O157:H7. Because HUS cases generally come to medical attention, surveillance for HUS can serve as a marker for *E. coli* O157:H7 activity in the community and may lead to the identification of outbreaks at the state or local level. HUS is also an important event for assessing morbidity caused by *E. coli* O157:H7.
- To identify whether the case may be a source of infection for other persons (*e.g.*, a diapered child, daycare attendee or foodhandler) and, if so, to prevent further transmission.
- To identify transmission sources of public health concern (*e.g.*, a restaurant or a commercially contaminated food product) and to stop transmission from such sources.

B. Laboratory and Healthcare Provider Reporting Requirements

Refer to the lists of reportable diseases (at the end of this manual's Introduction) for specific information.

Note: Due to the potential severity of HUS, the Massachusetts Department of Public Health (MDPH) requests that information about any suspect or known case of HUS be **immediately reported** to the local board of health where diagnosed. If this is not possible, call the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 (weekdays), or (617) 983-6200 (emergency number for nights/weekends). A case of HUS is defined by the reporting criteria in Section 2) A above.

C. Local Board of Health Reporting and Follow-Up Responsibilities

1. **Reporting Requirements**
   MDPH regulations (*105 CMR 300.000*) stipulate that each local board of health (LBOH) must report the occurrence of any case of HUS, as defined by the reporting criteria in Section 2) A above. Please refer to the *Local Board of Health Reporting Timeline* (at the end of this manual's introductory section) for information on prioritization and timeliness requirements of reporting and case investigation.

2. **Case Investigation**
   a. **The most important thing a LBOH can do if it learns of a suspect or confirmed case of HUS is to call the MDPH immediately, any time of the day or night.** Daytime phone numbers of the Division of

Epidemiology and Immunization are (617) 983-6800 and (888) 658-2850. The phone number for nights and weekends is (617) 983-6200.

b. Following notification of the MDPH, it is the LBOH responsibility to complete a *Hemolytic Uremic Syndrome Case Report Form* (in Appendix A). Much of the information required on the form can be obtained from the case's healthcare provider or the medical record. You may ask the case's healthcare provider to complete the case information in the case report form.

c. It is helpful to complete an *HUS Case Investigation Worksheet*. Information for this worksheet should be obtained from the case or the case's parent/guardian. Be sure to obtain as much information as possible about foods and activities during the week prior to the onset of the diarrheal illness (not HUS onset). (See also the chapters on *E. coli* O157:H7 and *Shigella* for more information on case follow-up.) *The worksheet does not replace the HUS case report form.*

d. Remember the following sections when completing the case report form:
   1) Accurately record the demographic/personal information.
   2) Complete the HUS case information, including sections on HUS diagnosis, symptoms, laboratory findings, other medical information, and outcome.

e. If you have made several attempts to obtain case information, but have been unsuccessful (*e.g.*, the case or healthcare provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the forms with as much information as you have gathered. Please note on the forms the reason why they could not be filled out completely.

f. After completing the case report form, attach lab report(s) and the *HUS Case Investigation Worksheet* and fax or mail (in an envelope marked "Confidential") to the MDPH Division of Epidemiology and Immunization, Surveillance Program. The confidential fax number is (617) 983-6813. Call the Surveillance Program at (617) 983-6801 to confirm receipt of your fax. The mailing address is:
   MDPH, Division of Epidemiology and Immunization
   Surveillance Program, Room 241
   305 South Street
   Jamaica Plain, MA 02130

g. Institution of disease control measures is an integral part of case investigation. It is the LBOH responsibility to understand, and, if necessary, institute the control guidelines listed below in Section 4), Controlling Further Spread.

4) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (*105 CMR 300.200*)

Foodhandlers with HUS must be excluded from work, although people diagnosed with HUS are usually hospitalized and too ill to be working. *Note:* A case of HUS is defined by the reporting criteria in Section 2) A of this chapter.

Minimum Period of Isolation of Patient

After symptoms have resolved, foodhandling facility employees may only return to work after producing one negative stool specimen. If a case has been treated with an anti-microbial, the stool specimen shall not be submitted until at least 48 hours after cessation of therapy. In outbreak circumstances, a second consecutive negative stool specimen will be required prior to returning to work.

Note: Because the onset of symptoms of HUS usually occurs about a week after diarrheal illness, stool cultures frequently fail to identify a causative agent.

Minimum Period of Quarantine of Contacts
Contacts with diarrhea who are foodhandling facility employees shall be considered the same as a case and handled in the same fashion. No restrictions otherwise.

Note: A foodhandler is any person directly preparing or handling food. This can include a patient care or child care provider. See glossary for a more complete definition.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Daycare
A case of HUS in a daycare setting may be a marker for additional *E. coli* O157:H7 or *Shigella* infections within the facility. Surveillance for gastrointestinal illness should be heightened and children with GI symptoms should be referred to their healthcare providers for appropriate testing. If the case has been diagnosed with *E. coli* O157:H7 or *Shigella* please refer to the appropriate chapter of this manual for that disease. The MDPH's *Health and Safety in Child Care* also provides guidelines for managing a gastrointestinal illness outbreak in a daycare setting. Contact the Division of Epidemiology and Immunization for assistance in managing follow-up of a case of HUS in a daycare setting.

School
A case of HUS in a school setting may be a marker for additional infections with *E. coli* O157:H7 or *Shigella* within the school, especially among classes with younger children. Surveillance for gastrointestinal illness should be heightened and students with GI symptoms should be referred to their healthcare providers for appropriate testing. If the case has been diagnosed with *E. coli* O157:H7 or *Shigella* please refer to the appropriate section of this manual for that disease. The MDPH's *Comprehensive School Health Manual* also provides guidelines for managing a gastrointestinal illness outbreak in a school setting. Contact the Division of Epidemiology and Immunization for assistance in managing follow-up of a case of HUS in a school setting.

Reported Incidence Is Higher than Usual/Outbreak Suspected
If the number of reported cases of HUS in your city/town is higher than usual, or if you suspect an outbreak, investigate to determine the source of infection and mode of transmission. A common vehicle (such as water, food or association with a daycare center) should be sought and applicable preventive or control measures should be instituted. Control of person-to-person transmission requires special emphasis on personal cleanliness and sanitary disposal of feces. Consult with the epidemiologist on-call at the Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several town lines and therefore be difficult to identify at a local level.

Note: Refer to the MDPH's *Foodborne Illness Investigation and Control Reference Manual* for comprehensive information on investigating foodborne illness complaints and outbreak. (Copies of this manual were distributed to local boards of health in 1997–98. It can also be located on the MDPH website in PDF format at <http://www.magnet.state.ma.us/dph/fpp/refman.htm>.) For recent changes (fall of 2000) to the Massachusetts Food Code, contact the Division of Food and Drugs, Food Protection Program at (617) 983-6712 or through the MDPH website at <http://www.state.ma.us/dph/fpp/>.

D. Preventive Measures

Environmental Measures
Implicated food items must be removed from the environment. A decision about testing implicated food items can be made in consultation with the Division of Food and Drugs (DFD) or the Division of Epidemiology and

Immunization. DFD can help coordinate pickup and testing of food samples. If a commercial product is suspected, DFD will coordinate follow-up with relevant outside agencies. DFD is reachable at (617) 983-6712.

Note: The role of the DFD is to provide policy and technical assistance with the environmental investigation, such as interpreting the Massachusetts Food Code, conducting a HACCP risk assessment, initiating enforcement actions and collecting food samples.

The general policy of the SLI is only to test food samples implicated in suspected outbreaks, not single cases (except when botulism is suspected). The LBOH may suggest that the holders of food implicated in single case incidents locate a private laboratory which will test food or to store the food in their freezer for a period of time in case additional reports are received. However, a single, confirmed case with leftover food consumed within the incubation period, may be considered for testing.

Note: Refer to the MDPH's *Foodborne Illness Investigation and Control Reference Manual* for comprehensive information in investigating foodborne illness complaints and outbreak.

Personal Preventive Measures/Education
To avoid future exposure, advise individuals to:

- Wash their hands thoroughly with soap and water before eating or preparing food, after using the toilet and after changing diapers.
- After changing diapers, wash the child's hands as well as their own.
- Dispose of feces in a sanitary manner, especially in daycare centers or other institutional settings.
- Scrub their hands thoroughly after assisting in the following: caring for someone with diarrhea, cleaning toilets, and changing soiled diapers, clothing or bed linens.
- Keep food that will be eaten raw, such as vegetables, from becoming contaminated by animal-derived food products.
- Send back all undercooked hamburger for further cooking.
- Cook all ground beef and hamburger thoroughly.
- Drink only pasteurized milk, juice, or cider.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.

An *E. coli* O157:H7 *Public Health Fact Sheet* can be obtained from the Division of Epidemiology and Immunization or through the MDPH web site at http://www.state.ma.us/dph/. Click on the "Publications" link and scroll down to the Fact Sheets section. It is also available in Spanish.

ADDITIONAL INFORMATION

The following is the formal Centers for Disease Control and Prevention (CDC) surveillance case definition for HUS. It is provided for your information only and is not necessary to use this information for reporting or investigating a case. (CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting and may be used to uniformly define an outbreak of HUS.) For reporting to a case to the MDPH, always use the criteria outlined in Section 2) A of this chapter.

Laboratory criteria for diagnosis
The following are present at some time in the illness:

- Anemia (acute onset) with microangiopathic changes (*i.e.*, schistocytes, burr cells, or helmet cells) on peripheral blood smear.

- Renal injury (acute onset), evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., ≥ 1.0 mg/dL in a child aged < 13 years or ≥ 1.5 mg/dL in a person aged ≥ 13 years, or ≥ 50% increase over baseline)

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not <150,000/mm^3, other diagnoses should be considered.

Case classifications
Probable:

- An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding three weeks or
- An acute illness diagnosed as HUS or TTP, that a) has onset within 3 weeks after onset of acute diarrhea or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed.

Confirmed: an acute illness diagnosed as HUS or TTP, that both meets the laboratory criteria and began within 3 weeks after onset of an episode of acute or bloody diarrhea.

Comment
Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as post-diarrheal TTP also should meet the criteria for HUS. These cases are simply reported as post-diarrheal HUS.

REFERENCES

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